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Nickel Fluorocarbene Metathesis with Fluoroalkenes

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Abstract: Alkene metathesis with directly fluorinated alkenes is challenging, limiting its application in the burgeoning field of fluoro-organic chemistry. A new nickel tris(phosphite) fluoro-(trifluoromethyl)carbene complex ([P₃Ni]=CFCF₃) reacts with $CF_2=CF_2$ (TFE) or $CF_2=CH_2$ (VDF) to yield both metallacyclobutane and perfluorocarbene metathesis products, [P₃Ni]=CF₂ and $CR_2=CFCF_3$ (R = F, H). The reaction of [P₃Ni]=CFCF₃ with trifluoroethylene also yields metathesis products, [P₃Ni]=CF₂ and cis/trans-CFCF₃=CFH. However, unlike reactions with TFE and VDF, this reaction forms metallacyclopropanes and fluoronickel alkenyl species, resulting presumably from instability of the expected metallacyclobutanes. Density functional theory calculations (DFT-M06) and experimental evidence establish that the observed metallacyclobutanes are not intermediates to the observed metathesis products, highlighting a novel variant of the Chauvin mechanism enabled by the disparate four-coordinate transition states.

Metal-catalyzed alkene metathesis is an immensely valuable C–C bond-forming method in organic synthesis.¹ This process involving fluoroalkenes could be an appealing option for obtaining new hydrofluoroalkenes which have recently been identified as low global warming potential refrigerants and blowing agents.² Metathesis traditionally produces new alkenes, polymers and organic compounds through the widely accepted [2+2] cycloaddition/retro-cycloaddition pathway (Chauvin mechanism; Scheme 1).¹ Computational studies suggest that this mechanism would be problematic for fluoroalkenes using typical Ru catalysts, as confirmed experimentally.3,4 Although recent elegant work has shown that cross-metathesis of fluoroalkenes and electron-rich alkenes can be accomplished with both Ru and Group 6 catalysts,^{5,6} addition of metal fluorocarbenes to electron-poor fluoroalkenes will likely require the former to be strongly nucleophilic. In light of the strong M-C^F bonds formed by second- and third-row transition metals, we have targeted



d⁹ [Ni=CF₂]⁺ may effect selected fluoroalkene metathesis reactions depending on the thermodynamic stability of the resulting fluoroalkene and Ni fluorocarbene partners.^{10,11} We recently reported the first examples of d¹⁰ Ni fluorocarbenes and their much faster (vs. Co) cycloaddition reactions with tetrafluoroethylene (TFE).^{8,9} We now report the first Ni=CF(CF₃) carbene complexes and show their reactivity towards fluoroalkenes.

The Chauvin mechanism, involving a high-energy metallacyclobutane intermediate, has been the mainstay for our understanding of metathesis activity and selectivity using both homogeneous and heterogeneous catalysts.^{1,3} In contrast, we have demonstrated that the cycloaddition reaction of Co fluorocarbene complexes with TFE involves a high-energy diradical intermediate followed by formation of a very stable metallacyclobutane (ca. 30 kcal/mol below starting materials).12 The difference in energy between [M]=CF₂/TFE reactants (M = Co, Ni) and the metallacyclic products is sufficiently large that metathesis reactions following the Chauvin mechanism are likely unfeasible for these systems. In this work we show that a similar mechanism is in play for the Ni=CF(CF₃) carbene and several fluoroalkenes (CR₂=CF₂; R = H, F) to from stable metallacyclobutanes, whereas a novel, parallel reaction pathway affords the metathesis products Ni=CF₂ + R₂C=CF(CF₃). In addition, analogous reactions of trifluoroethylene (TrFE) afford both metathesis products and products derived presumably from unstable metallacyclobutanes. The thermodynamics and mechanistic pathways of these unprecedented transformations have been examined by density functional theory (DFT) methods (M06).

The new fluoro(trifluoromethyl)carbene complex Ni[P(O-*i*-Pr)₃]₃(=CFCF₃) (1) was obtained from the reaction of Ni[P(O-*i*-Pr)₃]₄ with Cd(CF₂CF₃)₂·DME (DME = 1,2-dimethoxyethane)^{13,14} (Scheme 2; ~40% isolated yield).^{15,16} Our synthetic approach is similar to that developed by Roper and coworkers for making precious metal difluorocarbenes [M⁰]=CF₂; M = Ru, Os).^{10c,17} Analogous reactions with other NiL₄ complexes {L = PPh₃, P(OMe)₃, P(OPh)₃, CN[2,6-Me₂(C₆H₃)], CO} failed to give the corresponding NiL₃(=CFCF₃) compounds in greater than trace amounts.



Scheme 2

nucleophilic first-row metal fluorocarbenes and recently demonstrated their [2+2] cycloaddition to fluoroalkenes.^{7,8,9} In fact, early gas phase work by Beauchamp et al. suggested that

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Complex **1** reacts with TFE (1.6 equiv, room temperature in C_6D_6 , < 20 min) to yield trifluoromethyl-substituted perfluoronickelacyclobutane **2** (Scheme 3). Significantly, CFCF₃/CF₂ metathesis products are also observed in the same reaction mixture; specifically, hexafluoropropene (HFP) and a new nickel difluorocarbene (**3**). The ratio of metallacycle to [Ni]=CF₂ is ~ 9:1 for this system. Additionally, the reaction is significantly retarded upon addition of excess phosphite without affecting the product ratio, suggesting that both products are formed via a dissociative mechanism.



To assess the effect of hydrogen substitution on the alkene, we showed that reaction of 1 with 1,1-difluoroethylene (CF2=CH2, VDF) also gives metathesis and metallacyclobutane products (Scheme 3; R = H).²⁴ Note that the alkene generated by the metathesis pathway, $CH_2=CFCF_3$, is the industrially relevant refrigerant HFO-1234yf.¹⁸ Compared to the TFE reaction, metathesis products now constitute a larger proportion of the product mixture (2b:3 \approx 5:1), illustrating the sensitivity of the product distribution to the alkene substituents. For both reactions, the mass balance is near-quantitative: the metallacycle (2a or 2b) and nickel difluorocarbene (3) account for >95% of 1. Further, the ratio of metallacycle to metathesis products does not change with time, suggesting that the former is not an intermediate en route to the latter.¹⁹ This observation points to a non-traditional Chauvin mechanism for these metathesis reactions (see below).

Interestingly, the cycloaddition reaction of **1** with VDF produced a single regioisomer with the methylene fragment in the β -position of the metallacycle. This may be due to steric effects where the carbon with smaller substituents (CH₂ vs. CF₂) can approach the large Ni=CFCF₃ fragment more easily. However, if the metallacycle is derived primarily through the diradical mechanism of the cycloaddition reaction shown previously for Co,¹² it is also possible that the obtained regioisomer results from added stabilization of the diradical intermediate.²⁰

We further probed the effect of fluoroalkene substituents through reaction of **1** with 1,1,2-trifluoroethylene (TrFE) which again produced the expected metathesis products Ni=CF₂ and *cis/trans*-CHF=CFCF₃. However the expected metallacyclobutane products were not observed by ¹⁹F, ³¹P and ¹H NMR; instead metallacyclopropanes and fluoronickel alkenyl species



were obtained (Scheme 4). Assuming initial formation of the two regioisomeric metallacyclobutanes, we propose two routes for their further conversion. For major isomer **A** a 2,1-fluoride migration results in ring contraction to form the *E/Z*-isomers of (4) in a similar reaction to that reported previously for the Co perfluorinated variant using a Brønsted acid catalyst.⁷ The



driving force for these reactions is presumably formation of stable CF₃ groups (Scheme 5).²¹ In contrast, minor isomer B undergoes C-F bond activation by the Ni center, forming the E/Z-fluoronickel alkenyl isomers (5). Based on our previous work involving fluoride abstraction from fluorometallacyclobutanes^{7,9} and recent DFT studies on Ru carbenes²² a plausible mechanism for the formation of (5) is a β-fluoride abstraction from metallacycle B forming a Ni-F allyl complex, followed by a 1,3-fluoride shift (Figure S51). The detailed reaction pathway for this transformation is still under investigation. Although metallacycles A and B are not observed, calculations confirm their intermediate thermodynamic stability between those derived from TFE and VDF (see SI). In addition, the absence of products like 4 and 5 from reactions of 1 with either TFE or VDF^{23} suggests that the presence of a CHF moiety in the metallacyclobutanes allows for a lower energy transition state for the 2,1-F migration and C-F bond activation pathways. Assuming intermediate formation of 4 and 5, the metathesis products constitute almost 50% of the fluorine $[(4 + 5):3 \approx 2:1]$.

A related Ni fluorocarbene complex, Ni[P(OMe)₃]₃(=CFCF₃) (6), was synthesized through two-electron reduction^{8a,24} of a mixture of Ni(PPh₃)₂(CF₂CF₃)Br and P(OMe)₃ albeit with PPh₃ and other minor contaminants (¹⁹F NMR yield: 17%; Scheme 6). COMMUNICATION

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Figure 1: Reaction coordinate for reaction of 1 with TFE

Treatment of **6** with TFE afforded metathesis and metallacyclobutane products in a 1:1.4 ratio, demonstrating a significant ancillary ligand effect. In contrast, reaction of Ni(tripod)=CF(CF₃) complex (**7**)¹⁶ with TFE gave metallacycle with no metathesis products ([tripod = MeC(CH₂PPh₂)₃]; see SI).

To further understand these observations, we investigated these reactions in more detail using density functional theory

 $Ni(PPh_{3})_{2}(CF_{2}CF_{3})Br \xrightarrow{1) 3 P(OMe)_{3}}{2) 2.2 KC_{8}} (MeO)_{3}P...,Ni (MeO)_$

Scheme 6

(DFT) approaches employing the M06 functional.^{21,25,26,27,28,29} In the reaction between TFE and **1** both reactants have singlet ground states, and the ancillary ligand P(O-*i*-Pr)₃ has a low free energy of dissociation of 0.5 kcal/mol from Ni[P(O-*i*-Pr)₃]₃(=CFCF₃). Hence we propose that the reaction initiates with loss of P(O-*i*-Pr)₃ and subsequent interaction of Ni[P(O-*i*-Pr)₃]₂(=CFCF₃) with TFE (Figure 2).³⁰ The calculated results reveal two independent pathways under experimental conditions, which can lead to metathesis and metallacycle products, respectively.

In the metathesis pathway (blue in Figure 2), TFE binds weakly to the nickel center in IM_0 through both C atoms leading to transition state TS_1 , located 19.0 kcal/mol above the reactants, and intermediate IM_1 , about 4.9 kcal/mol higher than the reactants, in which the TFE C2–C3 bond is elongated by back-bonding from the electron-rich Ni center. Further elongation of the C2–C3 bond that accompanies formation of bicyclic transition state TS_2 (about 10.9 kcal/mol above the reactants) occurs in a plane that is *perpendicular* to that of the ancillary phosphite ligands. This unusual strained bicyclic intermediate is high enough in energy to prevent the complex from going through the highly downhill formation of the metallacycle, *vide infra* (Scheme 7).



The C2–C3 bond in TFE is then cleaved, with one –CF₂ residue bound to the Ni, while the other –CF₂ residue binds to carbene carbon C1 to produce P₁' (Δ G = -13.5 kcal/mol). Finally, metathesis products HFP and Ni[P(O-*i*-Pr)₃]₃(=CF₂) (P₁) are formed by exchange between the ancillary ligand and CF₂=CFCF₃, a process that is energetically favorable by 10.9 kcal/mol.

CFCF3

-44.4

CF2=

The unproductive metallacycle pathway (green in Figure 2), commences with the formation of an open-shell singlet diradical intermediate ($^{os}IM_0$) via one C atom of TFE weakly bonding with the carbene C atom, without the direct involvement of the metal. Formation of the C1–C2 σ bond (1.529 Å), through $^{os}TS_1$ ($\Delta G = 17.9$ kcal/mol) followed by low-energy rotation through $^{os}TS_2$ ($\Delta G = -5.8$ kcal/mol) around the newly-formed C1–C2 bond affords $^{os}IM_2$, another diradical intermediate that is slightly less stable than $^{os-1}IM_1$. Finally, metallacycle product P_{II} results from the C3–Ni diradical of $^{os}TS_3$ ($\Delta G = -7.8$ kcal/mol) with formation of the C3–Ni bond *in the same plane as the ancillary ligands* (see Table S1 for spin densities of the open-shell singlet species).

The metallacycle and metathesis products both exhibit remarkably low energies (-44.4 kcal/mol and -24.4 kcal/mol, respectively) relative to the starting materials. Thus, the pathways leading to metathesis products and metallacycle are too exothermic to be reversible. Since the rate-controlling transition states in both pathways, TS₁ and ^{os-1}TS₁, have comparable barriers (19.0 vs 17.9 kcal/mol), the product ratio will be determined by subtle differences in these transition states, as shown with the observed increase of metathesis products with ancillary ligand and upon replacement of C-F bonds (with C-H) from the metathesis partner. Moreover, to eliminate the possibility of this transformation progressing via a triplet state, it was calculated that for the rate-determining barrier, TS1, the open-shell singlet is significantly lower in energy than the closed-shell singlet (17.9 kcal/mol vs 22.6 kcal/mol), which is lower in turn than the triplet state (22.6 kcal/mol vs 24.1 kcal/mol). At the key intermediate IM1, the closed-shell singlet state is very unstable, while the open-shell singlet is still more stable than the triplet. After IM1, the open-shell singlet and triplet are close in energy until the product, which is much more stable Angewandte Chemie International Edition

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as the singlet, confirming that the diradical mechanism is the most probable. (see experimental SI)

To summarize, we have demonstrated the first examples of metal fluorocarbene metathesis with fluoroalkenes, through a novel variant of the Chauvin mechanism enabled by the disparate four-coordinate transition states. These results extend our understanding of metathesis mechanisms beyond the original Chauvin postulate, in which the metallacycle is an intermediate en route to metathesis products.1

Despite the important advances described herein, considerable challenges still face metal-mediated polyfluoroalkene metathesis. First, a more general source of nucleophilic metal carbenes is needed.³¹ Second, ground state energy differences between the Ni=CF $_2$ and Ni=CFCF $_3$ carbene complexes introduce additional barriers to efficient metal-catalyzed fluoroalkene metathesis that will require careful selection of the carbene/fluoroalkene partners. Ongoing experimental and computational efforts are focused on finding more systems that favor the metathesis pathway.

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contaminant being the starting material, Ni[P(O-i-Pr)₃]₄. Sublimation gave marginally improved purity but significantly diminished yield. See Supporting Information.

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